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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,914	03/02/2004	Fengxia Qi	UAB-17404/22	1392

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/790,914	QI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment and response filed July 28, 2005 are acknowledged. Claim 9 has been amended. Claims 15-28 have been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections/Rejection Withdrawn

3. In view of Applicant's amendment and response the following objections and rejections have been withdrawn:

a) objection to the specification, page 2 , paragraph 2 of previous Office action.

b) Rejection of claims 9-14 under 35 U.S.C. 112, first paragraph, page 2-7, paragraph 3 of previous Office action.

Rejection Maintained

4. The rejection under 35 U.S.C 102(b) is maintained for claims 9-10 for the reasons set forth on page 8, paragraph 4 of the previous Office Action.

Loyola-Rodriguez et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water of these animals (see the Abstract). Loyola-Rodriguez et al teach that mutacin may be a candidate for use in dental caries prevention (see the Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Loyola-Rodriguez et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to

show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Loyola-Rodriguez et al cannot be used as an anticipatory reference. Applicant urges that mutacin I has a molecular weight of approximately 2364 daltons, is made up of 24 amino acids in mature form and is highly themostable. Applicant urges that mutacin MT6223 has a molecular weight of 6500 daltons and the chemical structure is unknown. Applicant urges that mutacin MT6223 was grown on liquid culture and not on TH/agarose plate.

Applicant's arguments filed July 28, 2005 have been fully considered but they are not persuasive. It is the Examiner's position that the prior art teaches the claimed method. It should be remembered that the claims recite open-ended claim language, i.e. "comprising". It should be remembered that the MPEP 2111.03:

The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.");< Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Therefore, the method of treating or preventing a gram-positive infection in a subject used in the prior art administers to subjects a composition which includes an

isolated and purified peptide having the amino acid sequence as set forth in SEQ ID NO:2. To address comments regarding culture medium, it should be noted that the instant specification at page 26 teaches that mutacin I was produced on a TH/agarose plate at levels that were too low for isolated. Applicant has not provide a side-by-side comparison of the claimed method with that of the prior art to show that the methods differ. Therefore, Loyola-Rodriguez et al anticipate the claimed invention.

New Grounds of Rejection Necessitated by Amendment

Claim Objection

5. Claim 17 is objected to for the following informality: "staphylococci" and "enterococci" should be changed to "Streptococcus" and "Enterococcus". Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claimed invention is directed to methods of treating and preventing gram-positive infections in a subject comprising administering to the subject an effective

amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO 2 or a pharmaceutically acceptable salt, ester or prodrug thereof.

The claimed invention encompasses a method of treating or preventing all gram-positive bacterial infections.

Pages 22-28 of the instant specification describes the isolation and purification of mutacin I. However, the specification fails to disclose methods of treating or preventing any or all gram-positive infections in a subject. Although the specification contemplates the broad spectrum use of mutacin I can be used to treat against a variety of microorganism, the specification fails to teach or disclose data that demonstrates that the amino acid sequence as set forth in SEQ ID NO: 2 can used to provide treat or protection against infections caused by any or all gram positive microorganisms. There is no disclosure of subjects that have been immunized using the claimed method nor is there a disclosure of challenge studies that have been conducted to established the amino acid sequence used in the claimed method has the ability to provide treatment or protection against any or all gram-positive infections.

The claimed method encompasses treating and preventing infections caused by all gram-positive bacteria. This includes gram-positive bacteria such as *Bacillus anthracis* and *Clostridium botulinum*. O'Brien et al *(American Family Physicians, May 1, 2003, 67, 9)* teach microbes that are used in bioterrorism include *Bacillus anthracis* and *Clostridium botulinum* (page 1928). O'Brien et al teach that familiarity with infectious agents of highest priority can expedite diagnosis and initial management and lead to a successful public health response to a bioterrorist attack (see the Abstract). O'Brien et

al has taught that gram-negative bacteria can be quite difficult to diagnosis as well as manage infections caused by these organisms.

The specification has not shown that mutacin I can be used to treat or prevent infections caused by all gram-positive microorganisms. The claimed invention broadly encompasses any infection or disease caused by any gram-positive microorganism.

The claims also broadly encompass all species within the of *Streptococcus, Staphylococcus* or *Enterococcus* genera. Koch et al (*Vaccine 22, 2004, pages 822-830)* teach that the emergence of resistance against multiple antibiotics and the increasing frequency with which *Enterococcus faecalis* and *Enterococcus faecium* are isolated from hospitalization patients underscore the necessity for a better understanding of the virulence mechanisms of this pathogen and the development of alternatives to current antibiotic treatments (see the Abstract). Koch et al teach that enterococci are intrinsically not as virulent as other gram-positive organisms such as *Staphylococcus aureus*, pneumococci or group A streptococci which makes the study of their pathogenicity more difficult (page 822). Koch et al teach that the rapid increase in enterococcal strains resistant to vancomycin and other antibiotics and their ability to pass this trait on to other pathogens, i.e. *Staphylococcus aureus* indicates an urgent and expanding clinical problems (page 822).

The above mentioned infections/diseases are only a few of the microorganisms that are encompassed by the claimed invention and represent a small subset of the many diseases that exist that have no vaccine that is effective in treating and/or preventing such infectious diseases. The specification has not shown that mutacin I can

be used to treat or prevent infections caused by any gram-positive microorganism much less microorganisms of the genus *Staphylococcus* or *Enterococcus.* The pharmaceutical compositions used in the claimed method would not provide treatment or prevention against any gram-positive bacteria. The specification has not provided enablement for the claimed method since there are no working examples in the instant specification that demonstrate effectiveness of the peptide against all gram-positive microbial infections .nor has the instant specification enabled the use of mutacin I to treat or prevent infections caused by microorganisms of the genera *Staphylococcus* or *Enterococcus*. One skilled in the art would have to possess the knowledge or be provided with sufficient guidance to determine if the pharmaceutical compositions would reach the target microorganisms in order to treat or prevent infection.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect using the amino acid sequence as set forth in SEQ ID NO:2 to treat or prevent all gram-positive infections, 3) the

relative skill of those in the art is commonly recognized as quite high (post-doctoral level). It would require undue experimentation by one of skill in the art to determine whether the pharmaceutical compositions used in the claimed method would be effective in treating or preventing any gram-positive microbial infection or disease. One of skill in the art would require guidance, in order to practice the claimed invention in a manner reasonable in correlation with the claims. Without proper guidance, the experimentation is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 17-28 recite the term "pneumococci". It is unclear as to what the applicant is referring since "pneumococci" is not a genus of organisms. Correction/clarification is required.

Status of Claims

8. No claims allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
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October 7, 2005

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